Journal of Life Sciences & Biomedicine, vol. 3(76), No 1, p. 108-115 (2021)

Comparative analysis of *KRAS* and *NRAS* gene mutations in colorectal cancer

B.I. Bayramov[1]*, Sh.A. Mammadova[2], F.A. Gahramanova[2], N.Y. Bayramov[2]

[1]*Genetic Resources Institute of Azerbaijan National academy of Sciences, 155 Azadlig Ave., Baku AZ1106, Azerbaijan*
[2] *Department of Surgical Diseases, Azerbaijan Medical University, 23 A.A.Bakikhanov Str., Baku AZ1022, Azerbaijan*
***For correspondence:** bayram-bayramov-90@hotmail.com*

Received: April 06, 2021; Received in revised form: May12, 2021; Accepted: June 21, 2021

Identifying the genetic profile of cancer by tumor biopsy has made progress in precision medicine. The study of the genetic profile of a tumor can help to choose the optimal treatment at the right time and identification of the cause of drug resistance. It is known that the biopsy is an invasive procedure, and it has some risks. That is why the development of non-invasive methods such as liquid biopsy is required. It is possible to determine circulating cancer cells (CTC) and circulating free tumor DNA (cfDNA) fragments with this technique. In the present study, *KRAS* and *NRAS* codon 12 and 13 mutations were compared in biopsy-derived DNA and liquid biopsy-derived cfDNA. The study included 26 patients with colorectal cancer. DNA extraction has been performed in Human Genetics Laboratory of the Genetic Resources Institute of ANAS, from biopsy material and plasma. Five (19.2%) mutations were detected in tumor DNA samples and 2 (7.7%) mutations in plasma cfDNA in the *KRAS* gene. Totally 3 missense mutations were detected in the *NRAS* gene. Two of these mutations (7.7%) were identified in tissue DNA samples and one of these (3.8%) in cfDNA. It was determined that the incidence of *KRAS* gene mutations in both tissue DNA and cfDNA samples was higher than *NRAS* gene mutations. Obtaining cfDNAs by liquid biopsy and particularly analyzing RAS gene family play a significant role in the early diagnosis, anti-EGFR therapy, selection of the right drugs, resistance, and the prognosis of the disease.

Keywords: *Cancer, liquid biopsy, gene, cfDNT, exon*

INTRODUCTION

Colon cancer is the second most common malignant tumor in the world and the second most common cause of death (Sung et al., 2021). Studies estimate that by 2030, the number of newly diagnosed patients worldwide will be 2.2 million and the number of deaths will be 1.1 million (Arnold et al., 2020). The disease is asymptomatic in the early stages, so it is important to use screening tests for the early detection of malignant tumors as well as precancerous lesions (Zhang et al., 2019; Shaukat et al., 2021). The American Cancer Society recommends a yearly colonoscopy and stool blood test for control after age 50 (Shaukat et al., 2021). Long-term inflammatory diseases of the intestines, smoking, alcohol, malnutrition and some other factors play an important role in the etiology of the disease (Bayramov and Safiyeva, 2019). Studies have indicated that increasing the intake of red meat and fats in the daily diet, reducing the consumption of low-fiber foods, as well as fruits and vegetables increase the risk of disease (Larsson and Wolk, 2006; Haggar and Boushey, 2009; Aune et al., 2011). Factors such as obesity, lack of physical activity, diabetes, family history of disease also increase the risk of developing colon cancer (Haggar and Boushey, 2009; Cho et al., 2012; Deng et al., 2012). There are various oncogenes, tumor suppressor genes, cell cycle control genes, as well as epigenetic and genetic changes in DNA repair genes that play an important role in the molecular pathogenesis of colon cancer (Mahasneh et al., 2017).

Liquid biopsy has been used to analyze the genetic profile of circulating tumor cells (CTC) and

https://doi.org/10.29228/jlsb.14
Available online 30 June 2021

cell-free DNA fragments (cfDNA) and to monitor cancer in a non-invasive procedure (Normanno et al., 2018). Determination of nucleic acids in blood plasma and serum by minimally invasive methods has led to the emergence of modern approaches in the diagnosis and prognosis of colon cancer (Chen və Zhao, 2019). The heterogeneity of the malignant tumor has led to some difficulties in the choice of treatment or the use of tissue biopsy to monitor the disease (Wills et al., 2018). However, the liquid biopsy technique has the potential to eliminate the problem of tumor heterogeneity and to obtain information about the entire cancer genome (Cheung et al., 2018).

cfDNAs are small derivative DNA fragments that may contain mutations specific to cancer tissue and can be easily obtained from venous blood by liquid biopsy (Vymetalkova et al., 2018). The *KRAS*, *HRAS*, and *NRAS* genes are members of the RAS oncogenic family. The proteins encoded by these genes play important roles in cell division, differentiation, apoptosis and other cellular processes. Several organizations, such as the European guidelines and the National Comprehensive Cancer Network Guidelines for Oncology (NCCN) and the Food and Drug Administration (FDA), advise that patients with colorectal cancer who have any *KRAS* or *NRAS* gene mutations should not be treated with anti-EGFR monoclonal antibodies (Hamzehzadeh et al., 2018). The FDA has approved EGFR antibody therapy for patients without mutations in the 12th and 13th codons of the *KRAS* gene. The European Agency for Evaluation Medicinal Products (EMEA) has reported the use of cetuximab and panitumumab in colon cancer based on the analysis of exons 2, 3 and 4 of the *KRAS* and *NRAS* genes (Cutsem et al., 2009; Van Cutsem et al., 2011).

Analysis of genetic changes in the RAS (*KRAS*, *NRAS* and etc.) gene family and other oncogenes in plasma DNA can optimize the choice of target therapeutic drugs and anti-epidermal growth factor receptor (EGFR) therapy, especially for metastatic colorectal cancer. The aim of the current study was to compare *KRAS* and *NRAS* gene mutations in cfDNA fragments taken from blood plasma by liquid biopsy and tumor DNA samples obtained from tissue biopsy material in patients diagnosed with colorectal cancer.

MATERIALS AND METHODS

The study included 26 patients diagnosed with colon cancer at the Educational-Surgical Clinic of Azerbaijan Medical University. Preoperative blood samples were taken from the EDTA tube to obtain cfDNA from the patients included in the study. Patient information such as age, sex, diagnosis, results of pathohistological analysis, etc. registered at the clinic. DNA extraction from blood plasma and tumor biopsy was performed in the Laboratory of Human Genetics of the Genetic Resources Institute of ANAS according to QIAamp DNA Micro Kit protocol. Quantitative and qualitative indicators of DNA were also measured in Nanodrop (Thermo Scientific, 2000). For PCR amplification of *KRAS* and *NRAS* genes in a volume of 25 µl; 2.5 µl 10xPCR buffer, 2.5 µl $MgCl_2$ (50 mM), 0.25 µl dNTP mix (20 mM), 0.5 µl primers (10 pmol/µl), 0.25 µl Taq polymerase (5 U/µl), 2 µl genomic DNA (50 ng/µl) and 16.5 µl dH_2O were used, respectively.

The PCR (Applied Biosystems, USA) cycle conditions consisted of an initial denaturation step at 95˚C for 5 min, followed by 35 cycles at 95˚C for 45 sec, at 54˚C for 45 sec (*KRAS*) or at 58˚C for 30 sec (*NRAS*) and at 72˚C for 2 sec, with a final elongation step at 72˚C for 5 min. After 1.5% agarose gel electrophoresis, PCR amplicons were purified, followed by PCR for sequencing using the BigDye™ Terminator v3.1 Cycle Sequencing Kit. After this procedure, exon 2 of the *KRAS* and *NRAS* genes (codons 12 and 13) was analyzed with the Sanger 3730xL genome sequencer (Applied Biosystems) and the results were compared with the reference genome to identify mutations.

RESULTS AND DISCUSSION

Blood and tissue biopsies of 26 patients were analyzed in the current study. Fifteen (57.7%) of the study group were men and 11 (42.3%) were women. The age range was 39-84, and the average age was 61.9. The pathohistological results of the patients were T2 in 23.1%, T3 in 53.8% and T4 in 23.1%. Tumor grades were determined by pathohistological analysis of 7.7% G1, 73.1% G2 and 19.2% G3. Demographic and clinical parameters of patients are presented in Table 1.

A total of 7 mutations in the *KRAS* gene have been identified. Of these mutations, 5 (19.2%)

were found in tumor DNA samples and 2 (7.7%) in cfDNA. Four of the mutations in the tumor DNA (GGT>GAT, GGT>GTT, GGT>TGT and GGT>TTG) were found in the 12th codon of the 2nd exon of the *KRAS* gene, respectively.

Table 1. Demographic and clinical information of the study group

Characteristic	Study group N=26 (%)
Gender	
Male	15 (57.7%)
Female	11 (42.3%)
Age	
Range	39-84
Average	61.9±10.3
Tumor Stage	
T2	6 (23.1%)
T3	14 (53.8%)
T4	6 (23.1%)
Tumor Grade	
G1	2 (7.7%)
G2	19 (73.1%)
G3	5 (19.2%)

The 12th (GGT) and 13th (GGC) codons of the KRAS gene encode the amino acid glycine. As a result of mutations, the amino acid glycine was replaced by aspartic (Asp), valine (Val) and cysteine (Cys). The GGC> GGA heterozygous mutation in the 13th codon of the *KRAS* gene caused the conversion of valine to asparagine.

Table 2. Mutation spectrum of *KRAS* gene and their localization

Tumor	Codon	Mutation	Amino acid substitution
T1	12	GGT→GAT	Gly→Asp
T4	13	GGC→GAC	Gly→Asp
T6	12	GGT→GTT	Gly→Val
T12	12	GGT→TGT	Gly→Cys
T19	12	GGT→GTT	Gly→Val
Plasma			
P6	12	GGT→GAT	Gly→Asp
P21	12	GGT→GAT	Gly→Asp

Only in the cfDNA of the two samples a heterozygous mutation was detected in codon 12, and no mutation was found in the tissue DNA (Table 2). Figure 1 shows the electropherograms of sequencing analysis.

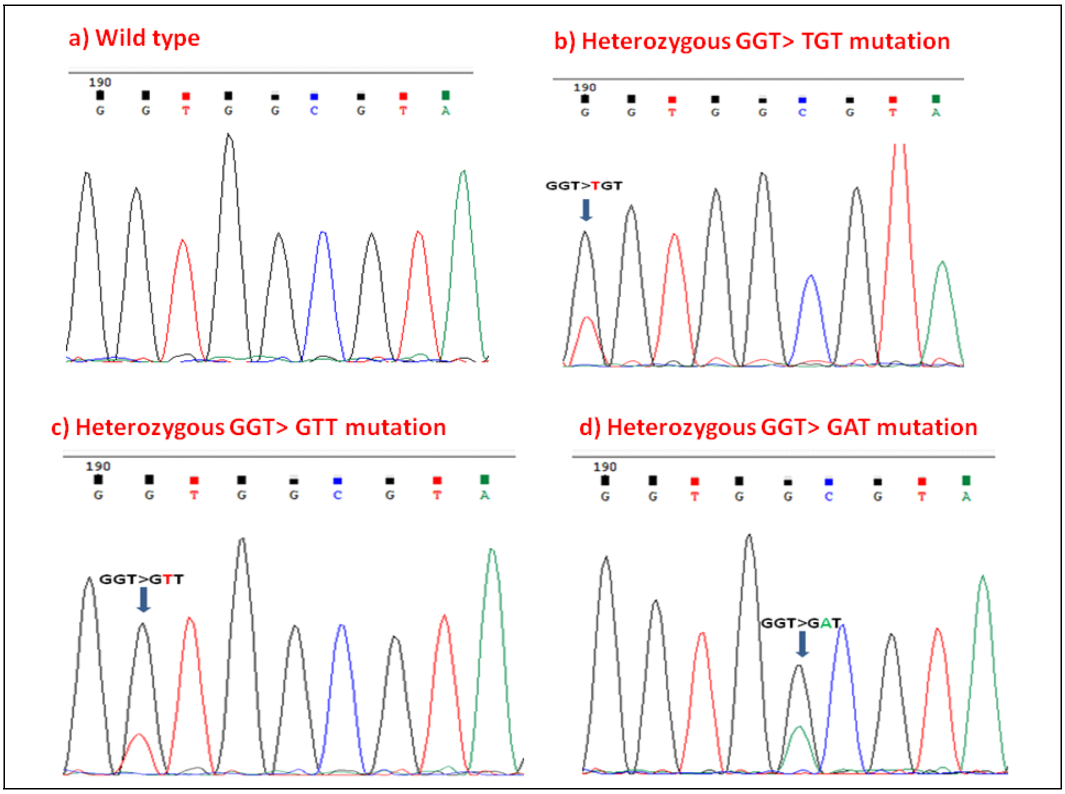


Fig. 1. Sanger sequence electropherogram of the 2nd exon of the *KRAS* gene.

Table 3. The spectrum of mutations in the 2nd exon of the *NRAS* gene and their localization

Tissue	Codon	Mutation	Amino acid substitution
T11	12	GGT→AGT	Gly→Ser
T26	12	GGT→GGG	Gly→Asp
Plasma			
Pl23	13	GGT→TGT	Gly→Cys

A total of 3 missense mutations were detected in 26 patients analyzed for the *NRAS* gene. Sequence analysis identified 2 mutations (7.7%) in tumor DNA and 1 (3.8%) mutation in cfDNA (Table 3). The missense mutation in tumor DNA samples was found in the 12th codon of the *NRAS* gene. In cfDNA (Pl-23), a missense mutation (GGT>TGT) was found in codon 13 of the *NRAS* gene, which caused the conversion of glycine amino acid to the cysteine. Figure 2 shows electrographic images of the *NRAS* gene.

One patient with a GGT>GAT missense mutation in exon 2 of the *KRAS* gene reported liver metastasis, while other patients with the mutation reported no organ metastasis. In cfDNA, in a patient with a GGT>TGT mutation of the *NRAS* gene, the tumor metastasized to both the liver and gallbladder. No metastases were reported in other patients with mutations in this gene.

Liquid biopsy is a minimally invasive technique used in recent years that allows for easy obtaining and analysis of circulating tumor cells (CTCs) and cfDNAs (Marrugo-Ramírez et al., 2018). Isolation analysis of cfDNA in blood plasma has advantages such as early diagnosis, monitoring of the response to therapy, in particular, clarification of the molecular mechanisms of drug resistance (Siravegna et al, 2014). Several biomarkers with widespread clinical use; *KRAS*, *NRAS*, *BRAF* mutations, Human Epidermal Growth Factor Receptor 2 (HER2) microsatellite instability (MSI), DNA repair (MMR) genes, etc. play an important role in choosing the optimal treatment (Afrăsânie et al., 2019). Mutations in codons 12 and 13 of KRAS gene exon 2 are found in 35-45% of cases of colorectal cancer and are considered to be the main predictor of resistance to anti-EGFR treatment (Therkildsen et al., 2014).

In our study, we analyzed 26 patients with colorectal cancer, 19.2% of *KRAS* gene mutations were identified in the biopsy material of patients, and 7.7% of missense mutations were detected on cfDNA. The frequency of mutations in the *NRAS* gene was 7.7% in cancer tissues and 3.3% in cfDNA samples, respectively. Erve et al. found that 54% of 100 patients had a *KRAS* gene mutation, 3% had a cfDNA mutation in a liquid biopsy, and no mutation was found in the *NRAS* gene (Erve et al., 2020).

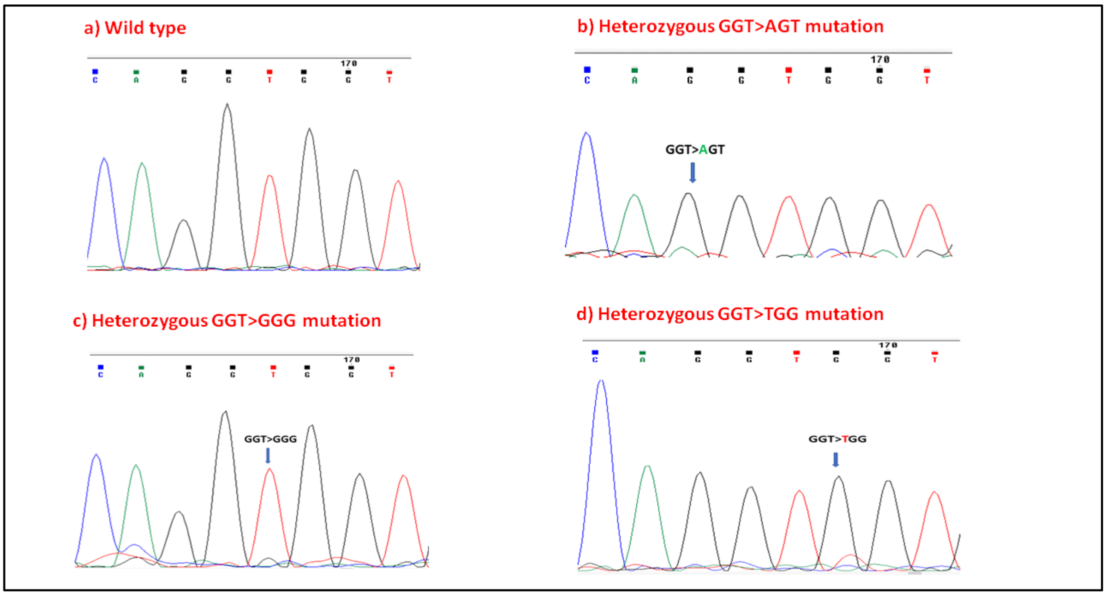


Fig. 2. Sanger sequence electropherogram of the 2nd exon of the *NRAS* gene.

In a study carried out in China in 2018, 50 genes were analyzed in both tumor tissue and cfDNA, a KRAS gene mutation was found in 27.7%, and liquid biopsy was recommended as a non-invasive diagnostic method (Yang et al., 2018). Takeda and colleagues found 47 mutations in cfDNA samples, of which 20 mutations were found only in cfDNA and not in tissue DNA (Takeda et al., 2019). Also, in our study, 2 mutations in the *KRAS* gene and 1 mutation in the *NRAS* gene were found only in cfDNA. This is explained by tissue heterogeneity and the specificity and sensitivity of the liquid biopsy. A study by the University of Montpellier in France found that the frequency of *KRAS*, *NRAS* and *BRAF* gene mutations was higher in cfDNA than in tumor DNA, suggesting that these tests could replace tissue biopsy (Thierry et al., 2017).

In conclusion, in our current study, we compared *KRAS* and *NRAS* gene mutations in both tissue DNA and cfDNA using liquid biopsy in patients diagnosed with colon cancer for the first time, using Sanger sequencing technology. *KRAS* gene mutations were found more frequently in patients compared to the *NRAS* gene. Analysis of *KRAS* gene mutations will enable the selection of the right treatment and obtaining optimal results, especially in patients with metastases. The use of liquid biopsy in medicine may be important in terms of early diagnosis, monitoring, treatment options, time-saving, and detection of new diagnostic biomarkers.

REFERENCES

Bayramov N., Səfiyeva A. (2019) Yoğun bağırsağın xoş xassəli törəmələrinin müalicəsinə müasir yanaşma prinsipləri. *Həyat Elmləri və Biotibb Jurnalı*, **74(2): 78-82**.

Arnold M., Sierra M.S., Laversanne M., Soerjomataram I., Jemal A., Bray F. (2017) Global patterns and trends in colorectal cancer incidence and mortality. *Gut,* **66(4):** 683-691.

Aune D., Chan D.S., Lau R., Vieira R., Greenwood D.C., Kampman E., Norat T. (2011) Dietary fibre, whole grains, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies. *BMJ*, **10:** 343:d6617.

Bao Q., He B., Pan Y., Tang Z., Zhang Y., Qu L., Xu Y., Zhu C., Tian F., Wang S. (2011) Genetic variation in the promoter of DNMT3B is associated with the risk of colorectal cancer. *Int. J. Colorectal Dis.*, **26(9):** 1107-1112.

Chen M., Zhao H. (2019) Next-generation sequencing in liquid biopsy: cancer screening and early detection. *Hum. Genomics*, **13(1):** Article ID 34.

Afrăsânie V.A., Marinca M.V., Alexa-Stratulat T., Gafton B., Păduraru M., Adavidoaiei A.M., Miron L., Rusu C. (2019) KRAS, NRAS, BRAF, HER2 and microsatellite instability in metastatic colorectal cancer - practical implications for the clinician. *Radiol Oncol.*, **53(3):** 265-274.

Cheung A.H., Chow C., To K.F. (2018) Latest development of liquid biopsy. *J. Thorac. Dis.*, **10:** S1645–S1651.

Cho E., Lee J.E., Rimm E.B., Fuchs C.S., Giovannucci E.L. (2012) Alcohol consumption and the risk of colon cancer by family history of colorectal cancer. *Am. J. Clin. Nutr.*, **95(2):** 413-419.

Marrugo-Ramírez J., Mir M., Samitier J. (2018) Blood-based cancer biomarkers in liquid biopsy: A promising non-ınvasive alternative to tissue biopsy. *Int. J. Mol. Sci.*, **19(10):** 2877.

Deng L., Gui Z., Zhao L., Wang J., Shen L. (2012) Diabetes mellitus and the incidence of colorectal cancer: an updated systematic review and meta-analysis. *Dig. Dis. Sci.*, **57(6):**1576-1585.

Erve I., Greuter M.J.E., Bolhuis K., Vessies D.C.L., Leal A., Vink G.R., van den Broek D., Velculescu V.E., Punt C.J.A., Meijer G.A., Coupé V.M.H., Fijneman R.J.A. (2020) Diagnostic strategies toward clinical ımplementation of liquid biopsy RAS/BRAF circulating tumor DNA analyses in patients with metastatic colorectal cancer. *J. Mol. Diagn.*, **22(12):**1430-1437.

Hamzehzadeh L., Khadangi F., Ghayoor Karimiani E., Pasdar A., Kerachian M.A. (2018) Common KRAS and NRAS gene mutations in sporadic colorectal cancer in Northeastern Iranian patients. *Curr. Probl. Cancer.*, **42(6):** 572-581.

Larsson S.C., Wolk A. (2006) Meat consumption and risk of colorectal cancer: a meta-analysis of prospective studies. *Int. J. Cancer.*, **119(11):** 2657-2664.

Mahasneh A., Al-Shaheri F., Jamal E. (2017) Molecular biomarkers for an early diagnosis, effective treatment and prognosis of colorectal cancer: Current updates. *Exp. Mol. Pathol.*, **102(3):** 475-483.

Normanno N., Cervantes A., Ciardiello F., De Luca A., Pinto C. (2018) The liquid biopsy in the management of colorectal cancer patients: Current applications and future scenarios. *Cancer Treat. Rev.*, **70:** 1-8

Shaukat A., Kahi C.J., Burke C.A., Rabeneck L., Sauer B.G., Rex D.K. (2021) ACG Clinical guidelines: Colorectal cancer screening. *Am. J. Gastroenterol.*, **116(3):** 458-479.

Siravegna G., Bardelli A. (2014) Genotyping cell-free tumor DNA in the blood to detect residual disease and drug resistance. *Genome Biol.*, **15:** 449.

Sung H., Ferlay J., Siegel R.L., Laversanne M., Soerjomataram I., Jemal A., Bray F. (2021) Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J. Clin.*, **71(3):** 209-249.

Takeda K., Yamada T., Takahashi G., Iwai T., Ueda K., Kuriyama S., Koizumi M., Matsuda A., Shinji S., Ohta R., Yokoyama Y., Hotta M., Hara K., Yoshida H. (2019) Analysis of colorectal cancer-related mutations by liquid biopsy: Utility of circulating cell-free DNA and circulating tumor cells. *Cancer Sci.*, **110(11):** 3497-3509.

Therkildsen C., Bergmann T.K., Henrichsen-Schnack T., Ladelund S., Nilbert M. (2014) The predictive value of KRAS, NRAS, BRAF, PIK3CA and PTEN for anti-EGFR treatment in metastatic colorectal cancer: A systematic review and meta-analysis. *Acta Oncol.*, **53(7):** 852-864.

Thierry A.R., El Messaoudi S., Mollevi C., Raoul J.L., Guimbaud R., Pezet D., Artru P., Assenat E., Borg C., Mathonnet M., De La Fouchardière C., Bouché O., Gavoille C., Fiess C., Auzemery B., Meddeb R., Lopez-Crapez E., Sanchez C., Pastor B., Ychou M. (2017) Clinical utility of circulating DNA analysis for rapid detection of actionable mutations to select metastatic colorectal patients for anti-EGFR treatment. *Ann. Oncol.*, **28(9):** 2149-2159.

Van Cutsem E., Köhne C-H., Hitre E., Zaluski J., Chang Chien C-R., Makhson A. (2009) Cetuximab and chemotherapy as initial treatment for metastatic colorectal cancer. *N. Engl. J. Med.*, **360(14):** 1408-1417.

Van Cutsem E., Köhne C-H., Láng I., Folprecht G., Nowacki M.P., Cascinu Sl. (2011) Cetuximab plus irinotecan, fluorouracil, and leucovorin as first-line treatment for metastatic colorectal cancer: updated analysis of overall survival according to tumor KRAS and BRAF mutation status. *J. Clin. Oncol.* (JCO), **29(15):** 2011-2019.

Vymetalkova V., Cervena K., Bartu L., Vodicka P. (2018) Circulating cell-free DNA and colorectal cancer: A systematic review. *Int. J. Mol. Sci.*, **19(11):** 3356.

Wills B., Gorse E., Lee V. (2018) Role of liquid biopsies in colorectal cancer. *Curr. Probl. Cancer.*, **42(6):** 593-600.

Yang Y.C., Wang D., Jin L., Yao H.W., Zhang J.H., Wang J., Zhao X.M., Shen C.Y., Chen W., Wang X.L., Shi R., Chen S.Y., Zhang Z.T. (2018) Circulating tumor DNA detectable in early- and late-stage colorectal cancer patients. *Biosci. Rep.*, **38(4):** BSR20180322

Zhang J., Haines C., Watson A.J.M., Hart A.R., Platt M.J., Pardoll D.M., Cosgrove S.E., Gebo K.A., Sears C.L. (2019) Oral antibiotic use and risk of colorectal cancer in the United Kingdom, 1989-2012: a matched case-control study. *Gut*, **68(11):** 1971-1978.

Yoğun bağırsağın bəd xassəli törəmələrində *KRAS* və *NRAS* gen mutasiyalarının müqayisəli tədqiqi

B.İ. Bayramov[1], Ş.A. Məmmədova[2], F.A. Qəhrəmanova[2], N.Y. Bayramov[2]

[1]AMEA-nın Genetik Ehtiyatlar İnstitutu, Bakı, Azərbaycan
[2]Azərbaycan Tibb Universitetinin I Cərrahi xəstəliklər kafedrası, Bakı, Azərbaycan

Toxuma biopsiyası nəticəsində xərçəng toxumasının genetik profilinin öyrənilməsi fərdiləşdirilmiş tibb sahəsində yeni irəliləyişlərin əldə olunmasına imkan yaratmışdır. Törəmənin genetik profilinin öyrənilməsi vaxtında düzgün müalicə seçimini və dərman rezistentliyi səbəbinin aşkarlanmasını təmin edə bilir. Buna baxmayaraq, biopsiya prosedurunun invaziv olması və müəyyən riskləri əhatə etməsi maye biopsiyası kimi invaziv olmayan metodların inkişaf etdirilməsinə zəmin yaratmışdır. Bu üsulla qanda sirkulyasiya edən xərçəng hüceyrələrini (CTC) və sərbəst şiş DNT (cfDNT) fraqmentlərini analiz etmək mümkündür. Cari tədqiqat işində biopsiya ilə alınan törəmə DNT-si və maye biopsiyası ilə əldə olunan cfDNT-də *KRAS* və *NRAS* genlərinin 12-ci və 13-cü kodonunda baş verən mutasiyalar müqayisəli tədqiq edilmişdir. Tədqiqat işinə yoğun bağırsaq xərçəngi diaqnozu qoyulan 26 xəstə daxil edilmişdir. Genetik analizlərin aparılması üçün biopsiya materialından və qan plazmasından AMEA Genetik Ehtiyatlar İnstitutu, İnsan Genetikası Laboratoriyasında DNT ekstraksiyası həyata keçirilmişdir. *KRAS* geni üzrə 26 şiş toxuması DNT nümunələrində 5 (19,2%) mutasiya, plazma cfDNT nümunələrində isə 2 (7,7%) mutasiya aşkar edilmişdir. *NRAS* geni üzrə isə ümumilikdə 3 missens tipli mutasiya aşkar edilmişdir. Analiz nəticəsində məlum olan mutasiyaların 2-si (7,7%) toxuma DNT nümunələrində, biri (3,8%) isə cfDNT-də müəyyən edilmişdir. *KRAS* gen mutasiyalarının həm toxuma DNT nümunələrində, həm də cfDNT-lərdə *NRAS* geni ilə müqayisədə rastgəlmə tezliyi yüksək olmuşdur. cfDNT-lərin maye biopsiyası vasitəsilə əldə olunması və xüsusilə də *RAS* gen ailəsinin analiz edilməsi erkən diaqnoz, anti-EGFR terapiyası, doğru dərman preparatlarının seçimi, rezistentlik və eləcə də xəstəliyin proqnozlaşdırılması baxımından mühüm əhəmiyyət kəsb edir.

Açar sözlər: *Xərçəng, maye biopsiyası, gen, cfDNT, ekzon*

Сравнительный анализ мутаций генов KRAS и NRAS при колоректальном раке

Б.И. Байрамов[1], Ш.А. Мамедова[2], Ф.А. Гахраманова[2], Н.Ю. Байрамов[2]

[1]Институт генетических ресурсов НАН Азербайджана, Баку, Азербайджан
[2] 1-ая кафедра хирургических болезней Азербайджанского медицинского университета, Баку, Азербайджан

Определение генетического профиля рака с помощью биопсии опухоли позволило достичь прогресса в сфере персонализированной медицины. Изучение генетического профиля рака может обеспечить правильный выбор лечения в нужное время и выявить причину лекарственной устойчивости. Известно, что биопсия - это инвазивная процедура и она сопряжена с определенными рисками. Вот почему необходима разработка неинвазивных методов, таких как жидкостная биопсия. С помощью этого метода можно проанализировать циркулирующие раковые клетки (CTC) и циркулирующие фрагменты свободной опухолевой ДНК (cfDNA). В этом исследовании сравнивали мутации в 12-м и 13-м кодонах генов KRAS и NRAS в ДНК, полученной из биопсии, и в cfDNA, полученной из жидкостной биопсии. В данное исследование были включены 26 пациентов с колоректальным раком. Выделение ДНК производилось в Лаборатории Генетики Человека Института Генетических

Ресурсов НАНА из биопсийного материала и плазмы. В гене KRAS 5 мутаций (19,2%) были обнаружены в образцах ДНК опухолевой ткани и 2 мутации (7,7%) в образцах cfDNA плазмы. Всего в гене NRAS обнаружено 3 миссенс-мутации. Две из этих мутаций (7,7%) были идентифицированы в образцах ДНК тканей и одна из них (3,8%) в cfDNA. Было установлено, что частота мутации гена KRAS, как в тканевой ДНК, так и в образцах cfДНК была выше, чем частота мутации гена NRAS. Получение cfDNA с помощью жидкостной биопсии и, особенно, анализ семейства генов RAS играет основную роль в ранней диагностике, терапии против EGFR, выборе правильных лекарств, устойчивости, прогнозировании заболевания.

Ключевые слова: *Рак, жидкая биопсия, ген, cfDNT, экзон*

ELM
NƏŞRİYYATI

Nəşriyyatın direktoru:	*Səbuhi Qəhrəmanov*
Kompüter tərtibçisi:	*Rəvanə İlmanqızı*
Bədii tərtibat:	*Şəlalə Məmməd*

Formatı 60x84 $^{1}/_{8}$
Həcmi 14,5 ç.v.
Tirajı 300

Ünvan: Bakı şəh., İstiqlaliyyət küç. 28